

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1-32727A/FMI	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 03/11554	International filing date (day/month/year) 17/10/2003	(Earliest) Priority Date (day/month/year) 18/10/2002
Applicant NOVARTIS FORSCHUNGSSTIFTUNG, ZWEIGNIEDERLASSUNG ..		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐

contained in the international application in written form.

☐

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority in written form.

☐

furnished subsequently to this Authority in computer readable form.

☐

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the title,☒

the text is approved as submitted by the applicant.

☐

the text has been established by this Authority to read as follows:

5. With regard to the abstract,☒

the text is approved as submitted by the applicant.

☐

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.☐

as suggested by the applicant.

☐

because the applicant failed to suggest a figure.

☐

because this figure better characterizes the invention.

☒

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/11554

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, PAJ, MEDLINE, EMBASE, WPI Data, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 66721 A (GOODYEAR LAURIE J; FLIER JEFFREY S (US); BETH ISRAEL HOSPITAL (US)) 9 November 2000 (2000-11-09) page 21, line 8 -page 24, line 22; claims 1-11	1-25
X	WO 01 44497 A (UNIV DUNDEE; ALESSI DARIO (GB); BIONDI RICARDO (GB)) 21 June 2001 (2001-06-21) page 58, line 1-3; claims 1,5,23,29,30,58 -/--	1-25

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

13 February 2004

Date of mailing of the international search report

25/02/2004

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
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Authorized officer

Stachowiak, O

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/11554

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ✓	PHAM PHUONG-TRUC T ET AL: "Assessment of cell-signaling pathways in the regulation of mammalian target of rapamycin (mTOR) by amino acids in rat adipocytes" JOURNAL OF CELLULAR BIOCHEMISTRY, vol. 79, no. 3, 7 September 2000 (2000-09-07), pages 427-441, XP002269150 ISSN: 0730-2312 abstract; figure 1	26
A	----	1-25
X ✓	FASSHAUER MATHIAS ET AL: "Hormonal regulation of adiponectin gene expression in 3T3-L1 adipocytes" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 290, no. 3, 25 January 2002 (2002-01-25), pages 1084-1089, XP002269151 ISSN: 0006-291X the whole document	26
A	----	1-25
A ✓	WO 00 08173 A (GOUT IVAN; YONEZAWA KAZU (US); HARA KENTA (US); WATERFIELD MIKE (U) 17 February 2000 (2000-02-17) abstract; claims 6,18,19	1-26
A ✓	WO 97 34137 A (LIVI GEORGE PETRO; MCLAUGHLIN MEGAN MCHALE (US); SMITHKLINE BEECHA) 18 September 1997 (1997-09-18) claims 1-59	1-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/11554

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11-17, and 23-25 are directed to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 10-15, 18-20 (all partly)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 10-15, 18-20 (all partly)

Claim 10 lacks clarity (Article 6 PCT) because in the absence of any structural feature of the claimed compound in the description or the claims, the skilled person cannot determine the scope of such a claim. Furthermore, an attempt is made to define the agent by reference to a result to be achieved, i.e., its identification by the claimed methods. Hence, the lack of clarity in the present case is such as to render a meaningful search of claim 10 over the whole claimed scope impossible. In a similar manner, claims 11-15, and 18-20 relate to methods and uses comprising an S6 kinase modulator or inhibitor compound without any structural feature. Thus, claims 10-15, and 18-20 have only been searched with respect to methods and uses comprising compounds or molecules specified in the description or the claims, i.e., with respect to antibodies, antisense molecules, ribozymes, and RNAs inhibiting S6 kinase activity.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/11554

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0066721	A	09-11-2000	AU 4683700 A	17-11-2000
			WO 0066721 A2	09-11-2000
			US 2003158139 A1	21-08-2003
WO 0144497	A	21-06-2001	AU 2187301 A	25-06-2001
			EP 1234188 A2	28-08-2002
			WO 0144497 A2	21-06-2001
			JP 2003516760 T	20-05-2003
			US 2003143656 A1	31-07-2003
WO 0008173	A	17-02-2000	AU 5333999 A	28-02-2000
			EP 1100929 A1	23-05-2001
			JP 2002525035 T	13-08-2002
			WO 0008173 A1	17-02-2000
WO 9734137	A	18-09-1997	EP 1017980 A2	12-07-2000
			JP 2000510327 T	15-08-2000
			WO 9734137 A2	18-09-1997
			US 6218136 B1	17-04-2001

PATENT COOPERATION TREATY

PCT


INTERNATIONAL PRELIMINARY EXAMINATION REPORT

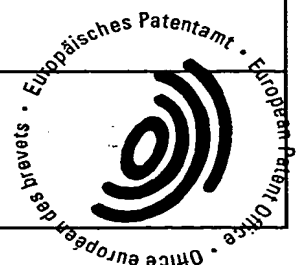
(PCT Article 36 and Rule 70)

(Rationalised Report according to the Notice of the President of the EPO published in the OJ11/2001)

Applicant's or agent's file reference 1-32727A/FMI	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP03/11554	International filing date (day/month/year) 17/10/2003	Priority date (day/month/year) 18/10/2002
International Patent Classification (IPC) or national classification and IPC C12Q1/48		
Applicant NOVARTIS FORSCHUNGSSTIFTUNG, ZWEIGNIEDER... et al.		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	<p>This REPORT consists of a total of <u> 2 </u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consists of a total of <u> </u> sheets.</p>
3.	<p>This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 23/04/2004	Date of completion of this report 18/08/2004
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer EIDEN F A Tel. (+49-89) 2399 2828



I. Basis of the report

The basis of this international preliminary examination is the application as originally filed.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question of whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable has not been the subject of the international preliminary examination in respect of the claims which have not been searched (Article 17(2)(a) or (3) and Rule 66.1(e) PCT); see also international search report).

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

To the extent that the international preliminary examination has been carried out (see item III above), the following is pointed out:

In light of the documents cited in the international search report, it is considered that the invention as defined in at least some of the claims, which have been the subject of an international search report, does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and/or to involve an inventive step (see international search report, in particular the documents cited X and/or Y and corresponding claim references).

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To:

NOVARTIS FORSCHUNGSSTIFTUNG
Zweigniederlassung Fried. Miescher
Institute for Biomedical Research
Maulbeerstrasse 66
CH-4058 Basel
SUISSE

Date of mailing (day/month/year)	25/05/2004
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Applicant's or agent's file reference 1-32727A/FMI	REPLY DUE: within 2 / 00 months/days from the above date of mailing
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International application No. PCT/EP03/11554	International filing date (day/month/year) 17/10/2003	Priority date (day/month/year) 18/10/2002
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International Patent Classification (IPC) or both national classification and IPC C12Q1/48

Applicant NOVARTIS FORSCHUNGSSTIFTUNG, ZWEIGNIEDER... et al.


1. This written opinion is the first drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application
3. The applicant is hereby invited to reply to this opinion.

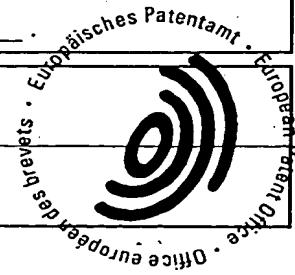
When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 18/02/2005

Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Examiner Formalities officer (incl. extension of time limits) Tel. (+49-89) 2399 2828
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I. Basis of the opinion

The basis of this written opinion is the application as originally filed.

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question of whether the claimed invention appears to be novel, to involve an inventive step, or to be industrially applicable has not been and will not be the subject of the international preliminary examination in respect of the claims which have not been searched (Article 17(2)(a) or (3) and Rule 66.1(e) PCT; see also international search report).

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability

1. To the extent that the international preliminary examination has been carried out (see item III above), the following is pointed out:
2. In light of the documents cited in the international search report, it is considered that the invention as defined in at least some of the claims, which have been the subject of an international search report, does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and/or to involve an inventive step (see international search report, in particular the documents cited X and/or Y and corresponding claim references).
3. If amendments are filed, the applicant should comply with the requirements of Rule 66.8 PCT and indicate the basis of the amendments in the documents of the application as originally filed (Article 34 (2) (b) PCT) otherwise these amendments may not be taken into consideration for the establishment of the international preliminary examination report. The attention of the applicant is drawn to the fact that if the application contains an unnecessary plurality of independent claims, no examination of any of the claims will be carried out.

NB: Should the applicant decide to request detailed substantive examination, then an international preliminary examination report will normally be established directly. Exceptionally the examiner may draw up a second written opinion, should this be explicitly requested.



INVESTOR IN PEOPLE

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Your Reference: 1-3272P1/FMI
Application No: GB 0224338.4
13 March 2003

Dear Sirs

Patents Act 1977: Search Report under Section 17(5)

I enclose two copies of my search report and a copy of the citations.

Plurality of invention

I consider that your application relates to more than one invention as follows:

Claims 1-7, 9 (in part) 10-16: relating to the use of S6 kinase modulators in obesity
Claims 8, 9 (in part) & 20: relating to the identification of an agent effective in treating obesity
Claims 17-19: relating to a method of diagnosing a predisposition to obesity.

My search report relates to the first invention only. If you want any of the other inventions searched, you should file a separate Patents Form 9/77 for each invention.

Non-patentable matter

Claims 11, 12 and 20 relate to a method of treating weight disorders. Since obesity is described on page 1 as being a metabolic disease it is considered that these claims are not patentable by virtue of Section 4(2).

Scope of search

Claim 9 is directed to an agent identified by the method of claims 1-8. However, no such

[†]Use of E-mail: Please note that e-mail should be used for correspondence only.



INVESTOR IN PEOPLE

Application No: GB 0224338.4

Page 2

13 March 2003

agent is defined in the application thereby rendering the subject matter of said claims purely speculative and a mere statement of the goals to be achieved. No meaningful search can be carried out for such "reach-through" claims, the scope of which is open-ended and unclear. In addition, claims 13-15 refer to modulators of S6 kinase without giving a technical characterisation. Since no such modulators are defined in the application, the scope of these claim is speculative and obscure in scope and their subject matter is not sufficiently disclosed and supported. No search can be carried out for such claims.

Documents cited

Any of WO01/44497, WO00/08173 and WO98/18935 cited in combination with WO00/66721.

Publication

I estimate that, provided you have met all formal requirements, preparations for publication of your application will be completed soon after **9 March 2004**. You will then receive a letter informing you of completion and telling you the publication number and date of publication.

Amendment/withdrawal

If you wish to file amended claims for inclusion with the published application, or to withdraw the application to prevent publication, you must do so before the preparations for publication are completed. **No reminder will be issued.** If you write to the Office less than 3 weeks before the above completion date, please mark your letter prominently: **"URGENT - PUBLICATION IMMINENT"**.

Yours faithfully

Dr Jeremy Kaye
Examiner



INVESTOR IN PEOPLE

Application No: GB 0224338.4
Claims searched: 1-7, 10-12 & 16

Examiner: Dr Jeremy Kaye
Date of search: 12 March 2003

Patents Act 1977 : Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance	
X, Y	X: 1-7, 10-12 & 16 Y: 1-7, 10-12 & 16	WO 00/66721 A2	(BETH ISRAEL DEACONESS MED. CENTER) see whole document
Y	1-7, 10-12 & 16	WO 01/44497 A2	(UNIV. DUNDEE) p.1, 1.5 - p.6, 1.22; claims
Y	1-7, 10-12 & 16	WO 00/08173 A1	(LUDWIG INST.) p.1, 1.26 - p.5, 1.27; claims
Y	1-7, 10-12 & 16	WO 98/18935 A2	(NOVARTIS AG) p.3, ll.19-25

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^v:

Worldwide search of patent documents classified in the following areas of the IPC¹:

C12N

The following online and other databases have been used in the preparation of this search report:

EPODOC, WPI, PAJ, BIOSIS, CAPLUS, EMBASE, MEDLINE, SCISEARCH